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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,024	12/11/2003	David B. Weiner	UPVG0005-101	2356
52308	7590	11/19/2008		
Pepper Hamilton LLP 400 Berwyn Park 899 Cassatt Road Berwyn, PA 19312-1183			EXAMINER HUMPHREY, LOUISE WANG ZHIYING	
			ART UNIT 1648	PAPER NUMBER
			MAIL DATE 11/19/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/734,024	<b>Applicant(s)</b> WEINER ET AL.	
	<b>Examiner</b> LOUISE HUMPHREY	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 August 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21-23 and 32-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-23 and 32-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This Office Action is in response to the amendment filed 19 August 2008. Claims 1-20 and 24-31 have been cancelled. Claims 21-23 and 32-34 are pending and currently examined.

#### ***Claim Objections***

The objection to claim 21 is withdrawn in response to Applicant's amendment.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 21-23 and 32-34 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement is maintained.

Claims 21-23 and 32-34 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and

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*Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention is the inhibition and prevention of lymphocyte activation by Vpr protein. The breadth of the claims encompasses both B lymphocytes and T lymphocytes and both *in vitro* and *in vivo* prevention and inhibition.

The disclosure fails to provide any working embodiments that meet the claimed limitations. While there are examples of assays to identify Rip-I-binding fragments of Vpr that are inducers or inhibitors of glucocorticoid receptor (GR) type II complex translocation from cytoplasm to the nucleus, no *in vitro* or *in vivo* working example of any prevention or inhibition of lymphocyte activation is disclosed in the specification.

The specification provides no guidance regarding practice of the claimed methods. The specification refers generally to the Vpr's interaction with the glucocorticoid steroid biochemical pathway (page 22, line 26-37), that the expression of Vpr within the cell causes the cell to stop proliferating (page 5, line 31-35) and that Vpr inhibits cytokine production/secretion by T cells, B cells, and monocytes during immunoglobulin activation (page 10, lines 14-20). However, the disclosure is silent pertaining to specific method steps of inhibition and prevention of lymphocyte activation.

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The disclosure fails to provide any guidance pertaining to the structural characteristics or mechanisms of the interaction between Vpr and lymphocytes. The specification specifically discloses in more details and in working examples the use of Vpr or Rip-I-binding fragments of Vpr protein as transfection agent for the delivery of conjugated nucleic acid molecule or derivatives into the nucleus of a cell (page 36-37), which is not remotely related to inhibition or prevention of lymphocyte activation. Therefore, the disclosure does not correlate with the claimed method of preventing and inhibiting lymphocyte activation in vitro or in vivo, especially inside humans.

At the time the invention was made, successful implementation of lymphocyte activation inhibition and prevention with Vpr was not routinely practiced by those skilled in the art. Prior art only teaches T lymphocytes to secrete cytokines upon activation (Mosmann, 1997) and B lymphocytes to produce immunoglobulins once activated by cytokines (Paul, 1987). The only effect of Vpr expression within cells is the alteration of distribution of cells in the cell cycle and thereby mediating the prevention of cell proliferation (Rogel, February 1995). The prior art is unpredictable and fails to provide sufficient illumination pertaining to the mechanisms underlying inhibition and prevention of lymphocyte activation by the Vpr protein.

There is no specific guidance in the art or specification and no specific examples of the claimed method set forth in the specification. While Applicant is not required to set forth working examples, the specification must set forth sufficient teachings to allow one to practice the claimed invention. Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the

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specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 21 (C.C.P.A. 1976). There is no evidence that Vpr has any effect on T lymphocyte secretion of cytokines, let alone any effect on the activation of B lymphocytes. Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue and unpredictable experimentation from the skilled artisan to practice the claimed invention.

In conclusion, the instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

### ***Response to Arguments***

Applicant's arguments filed 19 August 2008 have been fully considered but they are not persuasive. Applicant argues that the Office failed to set forth any reasoning or evidence to demonstrate that the claimed invention would not work. However, it is not the standard for Examiner to provide evidence showing inoperability of a claimed invention. Examiner reached the conclusion of undue and unpredictable experimentation to practice the claimed invention by evaluating the factors set forth by the court in *In re Wands* and *Ex Parte Forman* as indicated above. The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). See M.P.E.P. §2164.03 [R-2]. Relationship of Predictability of the Art and the Enablement Requirement. Since the

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prior art does not provide any teaching regarding the prevention and inhibition of lymphocyte activation by any viral protein, a significant amount of guidance or direction is needed to enable the claimed invention. Applicant did not disclose the underlying mechanisms in the lymphocyte cells after contacting with Vpr protein. There is no knowledge about the process of Vpr entering the lymphocytes leading to the inhibition and/or prevention of activation except for Applicant's theory that because Vpr interacts with lymphocyte Rip-1, which interacts with steroids, and hydrocortisone and dexamethasone inhibit activation of lymphocytes, Vpr must inhibit and prevent lymphocyte activation. The instant specification merely discloses Applicant's logical deduction to reach the claimed invention. Applicant has not provided any working example or data to demonstrate the effectiveness of contacting Vpr with lymphocyte cells to inhibit/prevent activation. The prophetic teachings of the specification are not supported by the art or evidence. Therefore, one skilled in the art would not be able to practice the claimed invention by only reading the specification.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./  
Examiner, Art Unit 1648  
17 November 2008

/Bruce Campell/  
Supervisory Patent Examiner, Art Unit 1648